

Griffith (J. P. S.) *al*
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IN FEBRILE AFFECTIONS.

BY

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Tetrahydroparachinanisol, or tetrahydroparamethyloxyquinolin, a hydrate of parachinanisol, was first synthetically prepared by Prof. Skraup, of Vienna, in 1884, and named by him "thallin," on account of the green color which its salts produce with the perchloride of iron (*θαλλος*, a green shoot).

It is a light powder of a pale yellow or almost white color, with a pleasant aromatic odor, resembling greatly that of the trailing arbutus. Its taste, however, is bitter, pungent, and disagreeable.

It is easily soluble in water, with difficulty in alcohol, and not at all in ether. The reaction of its solution is strongly acid. It is usually employed in the form of the sulphate or the tartrate of thallin, although other salts exist. Its chemical formula is $C_{10}H_{16}NO$. The reference to the paper containing a detailed description of the method of its manufacture will be cited below.

Von Jaksch was the first to experiment with it upon animals, and to apply it subsequently in medicine. Following him, various other clinicians made researches with the new drug, and reported their results, but up to the present time there has appeared, I believe, no published account of any clinical experiments with it, made either in this country or in Great Britain.

It was while watching its effect on fever, when given by v. Jaksch in the clinic of Nothnagel, before he had made his discovery public, that I first came to believe in the value of the drug as an antipyretic. And it is with the desire of bringing it more prominently and more favorably before the profession, that the investigations herein detailed have been made, and this communication written.

The first announcement from v. Jaksch was made to the *Wiener k. k. Gesellschaft für Aerzte*, in the fall of 1884, and published by him later. He followed this by several other papers on the same subject.

He shows that thallin is very similar in its effects to antipyrin, although in very much smaller doses; but claims that it is more rapid in its action, although the fall of temperature produced lasts for a shorter time. It is also less dangerous, inasmuch as it never causes collapse, as does the latter drug. Both agents may produce profuse sweating; and chilliness or rigors often occur with the subsequent rise of the temperature after the action of the medicines has ceased.

These conclusions he reached by giving thirty cases of various diseases, accompanied by fever, alternating doses of antipyrin and thallin. His investigations, throughout, were most careful and thorough. The usual dose of thallin as administered by him is four to

fifteen grains, given at one time, and repeated in one or two hours if no effect is produced. The degree of reduction of temperature obtained varies somewhat, and the duration of the lowered temperature lasts usually but a few hours.

He states that it can be detected in the urine by the dark red color which is produced on testing with the perchloride of iron. Before testing, too, a peculiar greenish shimmer may be seen at the edge of the receptacle.

Alexander, after experimenting on fourteen cases, confirms the favorable report of v. Jaksch. He gives the medicine in the same doses whenever the fever exceeds 102° F. This usually reduces the temperature to 101° or 101.5° , where it remains for two or three hours. On its again reaching 102° the dose is repeated, the patient receiving the drug four or five times in the course of the day. Very profuse perspiration is often produced, especially in cases of phthisis.

Huchard finds the temperature always reduced by four to twelve grains of thallin, with but slight accompanying perspiration, although shivering occurs frequently. He believes that it probably lessens the fever by acting on the thermogenetic centre.

Dujardin-Beaumetz, while admitting that thallin is the most powerful of antipyretics, considers it a poor member of the *materia medica*. He adopts the opinion of Brouardel and P. Loyer that it reduces the temperature by diminishing the respiratory power of the blood, and destroying the red blood corpuscles; and believes that antipyrin acts in an entirely different manner—*i. e.*, on the thermogenetic centre—and is much to be preferred.

This is the only really condemnatory criticism of the new antipyretic of which I am cognizant.

Guttmann's experience agrees with that of v. Jaksch, but he considers thallin to have many unpleasant secondary effects. Its action, too, he considers of too short duration, and he therefore gives the preference to antipyrin.

Ewald, on the other hand, says that the drug is safe, sure, and has no disagreeable secondary effects. He administers it in doses of four grains.

Landenberger reports seventy cases of various febrile affections to which he has administered the medicament. He gives it in from four to fifteen, usually eight grain doses, and in this way obtains a fall of temperature of even 5° or 7° F., accompanied by profuse sweating, but never by collapse or cyanosis. The effects continue five or six hours, before the mercury rises again. He usually administers it in wafers, to avoid the unpleasant taste, and has the temperature recorded hourly during the day, and every two hours at night.

He finds it much superior to antipyrin, kairin, and quinine, especially in reducing the temperature of erysipelas. It is also very efficacious in phthisis, but is apt to produce too profuse perspiration.

Stintzing, in employing thallin in Ziemssen's clinic, finds four grains sufficient to cause a fall of temperature of 1.5° to 3° F., lasting for three or four hours. The mercury then rises until it reaches the former or even a greater elevation. There is always more or less sweating after its use.

Mingazzini obtained better effects from a dose of eight grains than from smaller amounts. He never observed vomiting, collapse, or cyanosis, but sweating seldom fails to appear. He prescribes it either

by the mouth, hypodermatically, or in clyster, and produces a fall of temperature equalling 1.5° to 4.5° F., and lasting four to eight hours.

Jaccoud has made a very careful series of investigations on seventeen cases. His average dose is six to eight grains, and his maximum fifteen grains, administered in wafers. The drug was always given at 11 A.M., and the temperature recorded hourly until 6 P.M. He believes that the initial dose should always be small, of three or four grains or less, since the effect appears to depend more upon the individuality of the patient, than upon the actual amount of the drug employed. The same observation is true of antipyrin. He finds that the temperature falls 3° to 9° F., and, having once reached its lowest point in one and a half to three hours, at once begins to rise again, there being no persistence of a minimum temperature. In two to four hours from the time the mercury begins its reascent, it attains its original elevation. Copious perspiration attends the reduction of the fever, and with the subsequent increase of the latter there is a sensation of chilliness and sometimes a rigor. His conclusions are that the salts of thallin are much to be preferred to antipyrin. With the latter drug the dose is much larger, the reduction of temperature not so great, and of no longer duration, the sweating more profuse, and chilliness and rigors more frequent. Then, too, there exists the disposition to the occurrence of the antipyrin-exanthem. He considers that liability to the development of collapse is equally great with both antipyrin and thallin. But the danger is much greater and more insidious from the former drug. Having once established the amount of thallin which can be given to a particular case, this dose can be employed without fear for as long a time as may be desired. But in the case of antipyrin the danger is renewed with every administration of the remedy. He has found by actual experience that a dose of antipyrin borne well on one day, may on another cause symptoms of collapse.

Pavay has employed thallin in seventeen cases and with a result almost diametrically opposed to that obtained by Jaccoud; much preferring antipyrin. Like v. Jaksch, he gave antipyrin and thallin alternately in a series of cases, and finds that of the two thallin produces much the greater sweating when eight grains of it are given. But it requires forty-five to sixty grains of antipyrin to lower the temperature to the same degree. The reduction of temperature after antipyrin lasts much longer, and rigors and collapse are not so likely to occur.

He disputes the statement of Dujardin-Beaumetz, and has repeatedly examined the blood without finding any alteration of the red blood-corpuscles after the use of thallin.

He gives four grains every quarter to half hour if the temperature exceeds 102° F. In one to two hours a fall of 3° to 5° F. is almost always obtained. He has endeavored in vain to check the profuse perspiration by administering one-sixty-fifth grain of atropia simultaneously with the antipyretic. After a dose of twelve grains of thallin he has observed collapse and more or less cyanosis. He agrees with Jaccoud that the drug is not to be invariably recognized in the urine by means of the perchloride of iron—a proof that it is largely consumed in the system.

Sara Welt, on the other hand, has never seen true collapse follow its use. The patient, although perhaps appearing somewhat cyanosed, feels well, and there is no diminution of strength. She has made in

the medical clinic of Eichhorst, in Zurich, careful observations on the effects on the system of both thallin and antipyrin, administered to a large number of cases. Four grains of thallin are given hourly until apyrexia is produced. There is less profuse sweating and less frequent vomiting after the use of thallin than follow antipyrin, but chilliness or rigors occur more frequently.

Ehrlich and Laquer, in a recent paper on the employment of thallin in typhoid fever, advocate an entirely new method of administering it. They admit that thallin has two disadvantages: 1st. Its action, though rapid, is too transient. 2d. Hyperprexia with rigors is apt to follow the cessation of its effect on the system.

Antipyrin, on the other hand, has a more gradual fall of temperature, and a more lasting effect with a slower reascension of the temperature curve. This is because thallin is absorbed with great rapidity, often affecting the system in ten or fifteen minutes, and its elimination begins in one-half to one hour. Antipyrin, on the contrary, is absorbed more gradually and does not appear in the urine until three hours after its administration (Maragliano).

Thus are explained the disadvantages of thallin, and also the *much greater danger* accompanying the exhibition of antipyrin claimed by Jaccoud, and fully agreed to by Ehrlich and Laquer.

They have limited their article to their experience with nineteen cases of typhoid fever, to which they gave thallin in small doses frequently and persistently repeated. Their method is as follows: Thallin tartrate is given in solution every hour during the day, and every two hours at night, and the temperature recorded every two hours. Six-tenths to one grain hourly is the initial dose, which, after two or three hours, is increased by one-tenth to one-eighth grain, and again by the same amount in two or three hours more.

In this manner the dose is gradually increased until a reduction of temperature of 1.5° to 2.5° F. is obtained, without, however, attempting to procure complete apyrexia, and carefully avoiding any unpleasant secondary symptoms. In this way they are enabled to escape entirely all rigors and excessive perspiration. They claim also that the subjective symptoms of the disease, especially those affecting the sensorium, are improved.

They have never observed collapse, and but rarely chilliness, which was caused by too large a dose. Vomiting occasionally occurs, due to the very unpleasant taste. As soon, therefore, as they have once determined the proper dose for a certain patient, they order the medicine in pill form. The digestive organs and the kidneys were never affected, and the exanthem of antipyrin never observed. Occasionally slight sweating takes place, but without being annoying to the patient.

Though not prepared to make a positive claim to that effect, yet they are led to conclude from their observations that thallin probably has a specific action on typhoid fever, often ameliorating the symptoms and appearing to hasten recovery.

There are several other articles on the subject to which I could not obtain access.

There will be found below a list of references to the literature, which I have tried to make complete.

The abstracts of the views of the various investigators quoted above, exhibit a considerable difference of opinion. Dujardin-Beau-

metz is the only one who really condemns the new antipyretic. Pavay thinks that it can never take a place equal to that of antipyrin; and Guttmann also prefers the latter drug. But, with these exceptions, the general verdict is that thallin is a most valuable, prompt and safe antipyretic. The majority also claim that there is less profuse sweating following the use of thallin, and that the medicine is much safer and more rapid in its action than antipyrin. The weight of opinion, however, goes to prove its only disadvantage to be that the reduction of temperature after its employment does not last so long as that produced by antipyrin; but even this is contested by many of the writers mentioned.

I report below a series of cases illustrative of the value of thallin as an antipyretic. In most of these the drug was administered in a single dose, usually of four grains. The variety of diseases is unfortunately, but unavoidably, not so great as could be desired. The temperature was, when possible, recorded every hour; often this was not possible. It is not, as a rule, quoted here for those days upon which no antipyretic was given.

CASE I.—Phthisis with hectic and night sweats.

Nov. 19, 1885.—7 P.M., 103.4°; 8, 103.2 (4 grains of thallin sulph.); 9, 99.8; 10, 100.6; 11, 100.8; 12, 101; 1 A.M., Nov. 20th, 100.6.

27th.—8.30 P.M., 102° (4 grains of thallin sulph.); 9, 100.2; 10, 99.8; 11, 99.4; 12, 99.

28th.—1 A.M., 98.4°; 2, 98.2; 3, 98.6; 4, 99; 5, 99.2; 6, 99.

Dec. 9.—7 P.M., 102.4°; 9, 101 (4 grains of thallin sulph.); 11, 100.6.

10th.—1 A.M., 100°; 3, 99.4; 5, 99.8.

11th.—7 P.M., 102°; 9, 101.8 (4 grains of thallin sulph.); 11, 100.2.

12th.—1 A.M., 99.4°; 3, 99; 5, 98.8.

14th.—9 P.M., 101.4° (4 grains of thallin sulph.); 10, 100.8; 11, 100; 12, 99.

15th.—2 A.M., 99.4°; 3, 98.8; 5, 99.6; 6, 99.4.

27th.—2.30 P.M., 104.2° (4 grains of thallin sulph.); 3.30, 101.4; 4.30, 99.8; 5.30, 99; 6.30, 99.2; 7.30, 99.8; 8.30, 100.2; 10.30, 101.4.

Profuse sweating, usually followed the administration of thallin to this patient. For several days, however, she was very positive that she slept better and felt better after the use of the medicine. Later in the disease, the subjective symptoms were not so favorable.

CASE II.—Phthisis with hectic and profuse night sweats. Man, aged twenty.

Nov. 20, 1885.—8.30 P.M., 103° (4 grains of thallin sulph.; at 8.40, copious perspiration, but not so great as usual); 9, 102; 9.30, 100.6; 9.50, 100.

For three nights this patient took four grains of thallin with excellent results. Slept better, felt better, and perspired less than usual.

Subsequent trial of the medicine seemed to increase the sweating. A short time after taking the drug he was always conscious of a tingling, burning feeling throughout his whole body.

CASE III.—Phthisis with night sweats. Woman, aged twenty.

Nov. 28, 1885.—8 P.M., 102° (4 grains of thallin sulph.); 10, 100.4; 11, 99.6; 12, 99.

29th.—1 A.M., 99°; 2, 98.4; 3, 98.2; 4, 98.4; 5, 98.4; 6, 100; 7, 100.

30th.—8 P.M., 102.4° (4 grains of thallin sulph.); 9, 101.2; 10, 101; 11, 99.6; 12, 98.2.

Dec 1.—1 A.M., 98°; 2, 98; 3, 99.2; 4, 99.4; 5, 99.8; 6, 99.2.

2d.—7 P.M., 102° (4 grains of thallin sulph.); 9, 100.4; 10, 100.6; 11, 100; 12, 99.2.

3d.—1 A.M., 98.8°; 2, 98.4; 4, 99; 6, 99.2.

14th.—9 P.M., 102.6° (4 grains of thallin sulph.); 10, 101.4; 11, 100; 12, 99.8.

15th.—2 A.M., 99.2°; 3, 99.8; 4, 99.4; 5, 99; 6, 100; 7, 102.

26th.—9 P.M., 102.2° (4 grains of thallin sulph.); 10, 101.8; 11, 100; 12, 99.6.

27th.—1 A.M., 99.2°; 2, 98.8; 3, 100; 4, 100.4; 5, 100.3; 6, 100.8.

Jan. 2, 1886.—9 P.M., 102.6° (4 grains of thallin sulph.) 10, 100.4; 11, 99.4; 12, 99.

3d.—1 A.M., 99.2°; 2, 99.6; 3, 100.8; 4, 100.4; 6, 100.8.

CASE IV.—Pyopneumothorax; septic. Man, aged twenty-five.

Dec. 2, 1885.—9 P.M., 103.4° (4 grains of thallin sulph.); 11.30, 98.4 (profuse sweating and some chilliness and depression of strength).

3d.—3.30 A.M., 101°; 6, 101; 9, 103.6 (4 grains of thallin sulph.); 12.15 P.M., 100.2 (not much perspiration, but subjective symptoms not improved); 2.30, 101; 4.30, 101.8; 5.30, 102.

5th.—8 P.M., 104.6° (4 grains of thallin sulph.); 10, 100.8.

6th.—12.30 A.M., 100°; 2, 101.6; 6, 101.6; 7, 103.

23d.—9 P.M., 104.4°; (4 grains of thallin sulph.); 10, 101.2 (free perspiration); 11, 100.4; 12, 100.

24th.—1 A.M., 100°; 2, 99.6; 5, 101.2; 6, 102.

Jan. 14, 1886.—9 P.M., 102.6° (4 grains of thallin sulph.); 12, 100.

15th.—2 A.M., 99.2°; 3, 99.2; 6, 101.6.

CASE V.—Typhoid fever in a girl aged fifteen; eighth day of the disease.

Dec. 4, 1885.—9.30 A.M., 105° (4 grains of thallin sulph.); 10.30, 102.4 (profuse sweat, pulse softer); 11.30, 102.6; 1.30 P.M., 105.6 (sponging with water and vinegar every hour); 6.30, 104.4.

5th.—9.50 A.M., 104.6° (4 grains of thallin sulph.); 10.30, 101 (perspiring; pulse soft); 11.30, 102; 1.30 P.M., 105 (2 grains of thallin sulph.); at 12.45 there was a slight chill, lasting half an hour, evidently ushering in the rise of temperature); 3, 102.6; 5, 105.7 (2 grains of thallin sulph.); 6.30, 103.8.

CASE VI.—Phthisis, advanced. Woman.

Dec. 5, 1885.—6 P.M., 101.5° (headache, gave 4 grains of thallin sulph.); 8, 97 (slight perspiration, feels better, and head aches less).

CASE VII.—Phthisis with nephritis and pyopneumothorax. Man, aged twenty-one.

Dec. 7, 1885.—5.15 P.M., 103.5° (4 grains of thallin sulph.); 5.45, 102.1 (at 5.40 a sensation of warmth over the whole body, and perspiration commencing; now profuse); 6.20, 100.4 (sweating entirely ceased); 7, 101.

CASE VIII.—Typhoid fever (seventh day) with pneumonia. Man, aged forty.

Dec. 8, 1885.—9.30 A.M., 103.4° (4 grains of thallin sulph.); 10.30, 100.8 (profuse perspiration); 11.30, 101; 1.30 P.M., 104.4; 2.30, 104.6 (4 grains of thallin sulph.); 3.30, 101.8 (profuse perspiration); 4.30, 102.1; 6.30, 104.4.

CASE IX.—Typhoid fever, second week. Man.

Dec. 18, 1885.—9.30 A.M., 102.4° (4 grains of thallin sulph.); 11, 98.4 (copious perspiration); 2 P.M., 102.5.

CASE X.—Phthisis. Woman, aged twenty-four.

Jan. 2, 1886.—9 P.M., 103.4° (4 grains of thallin sulph.); 10, 101.8; 11, 100.2; 12, 99.

3d.—1 A.M., 99.8°; 2, 99.6; 3, 101.8; 4, 101; 5, 101; 6, 103.2.

5th.—8 P.M., 103.4° (4 grains of thallin sulph.); 9, 101.8; 10, 99.5; 11, 98.4; 12, 100.

CASE XI.—Phthisis. Woman, aged twenty-eight.

Jan. 5, 1886.—1 P.M., 100°; 2, 100.8; 3, 100.6; 4, 101; 5, 101.4; 6, 102; 7, 102.4; 8, 103.2 (4 grains of thallin sulph.); 9, 101.2; 10, 99; 11, 98.2; 12, 99.2.

Feb. 1.—8 A.M., 100°; 8 P.M., 103.

2d.—8 A.M., 99.8°; 8 P.M., 102.6.

3d.—8 A.M., 99°; 8 P.M., 102.4 (administration of thallin tartrate, 6-10 grain every two hours, commenced).

4th.—8 A.M., 98.4° (6-10 grain of thallin tartrate hourly); 8 P.M., 100.

5th.—8 A.M., 98°; 8 P.M., 103 (thallin stopped at 10 A.M., Feb. 5th, on account of vomiting).

The temperature during the administration of the drug was recorded hourly, and showed a very marked reduction of the febrile temperature. Through an oversight, these records were destroyed.

CASE XII.—Phthisis. Man, aged twenty-two.

Jan. 14, 1886.—7 P.M., 104.2°; 9, 104.8 (4 grains of thallin sulph.); 10, 102.2; 11, 101 (considerable sweating); 12, 100.2.

15th.—1 A.M., 99.2° (chilliness); 2, 99; 3, 98.8; 4, 99.8; 5, 101.8; 6, 99.8; 7, 104.

19th.—7 P.M., 104°; 9.30, 106.6 (4 grains of thallin sulph.); 11.30, 99.6.

20th.—12.30 A.M., 99°; 1.30, 99; 2.30, 99; 5.30, 100.2.

CASE XIII.—Typhoid fever, fifth day. Man, aged twenty-one.

Feb. 10, 1886.—8 A.M., 102.4° (6-10 grain of thallin tartrate every hour); 10, 102; 12, 103.6; 2 P.M., 104 (dose increased to 8-10 grain hourly, and at night every two hours); 4, 104.4 (5 grains of thallin tartrate in one dose without effect); 6, 104.6 (the continuous use of 8-10 grain continued); 8, 104.4; 10, 103.4; 12, 103.6.

11th.—2 A.M., 102.4°; 6, 103.2; 8, 102; 10, 101; 12, 102 (dose of 1 grain of thallin tartrate substituted for 8-10 grain); 2 P.M., 103.8; 4, 103.2 (8 grains of thallin tart. in single dose, with but little sweating); 6, 102.2; 8, 101.4; 10, 102; 12, 102.2.

12th.—2 A.M., 102.6°; 4, 101.8; 6, 102; 8, 103; 10, 102 (dose increased to 1½ grains); 12, 103; 2 P.M., 103.4; 4, 102; 6, 103; 8, 103.4; 10, 103.2; 12, 103.2.

13th.—2 A.M., 103.2°; 4, 103.2; 6, 103.4; 8, 101.2; 10, 102; 12, 102.2; 2 P.M., 103; 4, 102; 8, 103; 10, 100.2; 12, 102.8.

14th.—2 A.M., 102.6°; 6, 103.4; 10, 101.4 (dose increased to 2 grains); 12, 103.5; 2 P.M., 102; 4, 102.6; 8, 103; 10, 103.4; 12, 102.

15th.—2 A.M., 104.6°; 4, 102.4; 6, 104.4; 10, 103.2 (thallin commenced 8 A.M., Feb. 10th, in continuous doses, now stopped); 12, 102.6; 2 P.M., 103 (20 grains of quinine); 3, 103; 3.30, 103.6; 4, 104; 4.30, 104; 5, 103.4; 5.30, 103; 6, 103; 6.30, 103; 7, 103; 7.30, 102.8; 8, 102; 8.30, 102.2; 9, 102.4; 9.30, 101.8; 10, 101.8; 12, 102.

16th.—2 A.M., 102°; 4, 102.2; 6, 102.2; 10, 101; 12, 103.4; 2 P.M., 103.4; 4, 104; (15 grains of antipyrin); 6, 101.2 (profuse sweat, more so than with thallin on Feb. 11th, *q. v.*); 8, 101.2; 9, 101.4; 11, 101.4.

17th.—10 A.M., 102°; 12, 103.2; 2 P.M., 103; 4, 103.4; 4.30, 104 (cold pack, with a slight temporary reduction of temperature); 8, 102.4; 10, 103.4; 12, 102.

18th.—2 A.M., 104.6° (15 grains of antipyrin); 4, 102.4 (profuse sweating); 6, 104.4; 8, 102.6; 10.30, 103.4; 11.30, 103.4 (cold pack, lasting 25 minutes with a fall of temperature at 11.55 in axilla, but a rise in the rectum); 11.55, 102.6; 2 P.M., 103.4; 3.30, 104.4 (8 grains of thallin sulph.); 4.45, 100 (profuse sweating and considerable depression); 8, 103.3; 10, 103.6; 12, 102.6.

19th.—2 A.M., 103°; 4, 103.4; 6, 103.6; 7, 104.

This case is particularly interesting as being an example of the greater efficiency of both thallin and antipyrin, as compared with quinine and the cold pack.

CASE XIV.—Pneumonia. Boy, aged twenty-two months.

Feb. 13, 1886.—1 P.M., 102.1° (¾ grain of thallin tartrate); 2.15, 101.4; 4, 103.9.

14th.—12.30 P.M., 103.2° (¾ grain of thallin tartrate); 2, 102.5; 3.15, 103.9 (1 grain of thallin tartrate); 4, 100.8.

CASE XV.—Pneumonia. Boy, aged twelve.

March 12, 1886.—4 P.M., 104.4° (2 grains of thallin sulph.); 5, 103.4; 5.15, 103.8; 7, 105.2.

14th.—8 A.M., 104.4°; 4 P.M., 104.2 (1½ grains of thallin sulph.); 6, 100.6.

CASE XVI.—Pneumonia. Boy, aged nine.

March 21.—4.30 P.M., 106.5° (3 grains of thallin sulph.); 5.30, 104.2; 6.30, 101; 9, 105 (3 grains of thallin sulph.); 12, 100.

22d.—6.30 A.M., 105°; 12.30 P.M., 104.8 (2 grains of thallin sulph.); 2, 102; 4, 105 (2 grains of thallin sulph.); 5, 103.4; 8, 103.

Thallin in both Cases XV. and XVI. not only reduced the temperature greatly while producing only moderate perspiration, but

diminished markedly the nervousness and restlessness and the rapid and violent heart's action. The condition of the sensorium was also decidedly improved, and the patients stated that they felt better. Sometimes natural sleep followed the use of the antipyretic. To both patients cold sponging was given hourly without any effect.

An inspection of the records given will show that thallin has been, without exception, efficacious in reducing temperature in the cases reported, and that this has usually occurred within one hour after its exhibition, although at times from two to three hours have been required before the full effect was obtained. Of course, no one claims that thallin or any other antipyretic is invariably successful.

The number of cases observed is sixteen, and the number of times the drug was administered, and the temperature recorded, exclusive of the continuous frequent exhibition of it in Cases XI. and XII.; equals forty-four. The dose usually given was four grains, which I have generally found sufficient. The greatest reduction of temperature obtained equals 7° F., and the least, 0.4° F.; the average being 2° to 4° F. The effect lasted a variable time, in the acute febrile affections not so long as in phthisis. In the latter disease, a dose of thallin administered in the evening sometimes occasioned a lowered temperature throughout the night. As a rule, it required two to five hours before the mercury reached its former elevation, if, indeed, it did ascend so high. I cannot agree with Jaccoud that the persistence of the minimum temperature equals *nil*. Profuse sweating was frequent, chilliness occurred but seldom, and a slight rigor was seen once. I have never observed collapse, but have seen depression of strength occur in two instances; due, I think, to excessive perspiration. Vomiting was produced in but one case, caused probably by the unpleasant taste of the medicine.

As to the subjective symptoms, some of the phthisical patients especially complained greatly; principally on account of the copious sweating. Others, however, experienced no unpleasant effects, and some felt decidedly better, slept better, and had less profuse perspiration than usual. Two cases perceived a peculiar sensation of warmth throughout the whole body soon after the ingestion of the drug.

My experience with the continuous administration of small doses, is limited to Cases XI. and XIII. Although unsuccessful in the later, I am inclined to believe that the remedy will often prove very efficacious when given in this manner.

Whether the simultaneous exhibition of atropia in sufficiently large doses will check the profuse perspiration forms not only an interesting clinical question, but bears upon the solution of the problem whether thallin simply causes a reduction of the surface temperature by evaporation, or acts upon the thermogenetic centre.

Thallin is undoubtedly a most powerful antipyretic, and the fact that decided depression of strength occurred twice in forty-four exhibitions of this remedy, indicated that it must be given with care to greatly debilitated subjects. It appears to have no particular action on the heart or on the respiration. As a rule, the rapidity of the respiratory movements and of the pulse is reduced at the same time with the degree of the fever, although not necessarily in proportion. With the question concerning the indications for the use of antipyretics in general, or the advisability of using them at all, these investigations have had nothing to do.

